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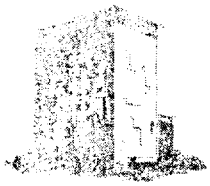

MEDICAL CENTER

McARDLE LABORATORY
FOR CANCER RESEARCH

UNIVERSITY OF WISCONSIN · MADISON, WISCONSIN 53706

February 29, 1980

Dr. W. J. Gartland, Jr.
ORDA
NIH
Bethesda, MD 20205

Dear Dr. Gartland:

As mandated by the 1978 and 1980 NIH Guidelines for Research Involving Recombinant DNA Molecules, I would like to propose the following major action to be included in the next Federal Register in the form of an I-D Exception and/or I-E-5 Exemption. In summary, the proposal is as follows: The present mandatory NIH Guidelines, including all regulations, inspections, applications and other bureaucratic and regulatory activities based on the so-called NIH Guidelines, should be suspended until such time that an "early warning" indicating any inadvertent harm caused by the recombinant DNA technique is noticed and scientifically verified.

For political reasons, the only experiments that might need permits (MUA) from the IBC or ORDA would be purposeful construction of pathogens (above class III) or other pests, and experiments leading to expression of potent toxins or other clearly harmful products, if done under conditions where there are convincing reasons to believe that some harm could be expected. The details of the latter classes could be worked out by a special RAC subcommittee.

The compelling reasons for accepting this proposal are manifold.

(1) It is an established fact that the recombinant DNA technique poses no true and present dangers. During the past nine years nobody has become sick or died, and no negative environmental affects have been produced by this technique.

(2) The risks of this technique are, therefore, only imaginary or speculative, similar to various science-fiction scenarios. Regulations based on only imaginary risks should certainly be suspended, especially since such "risks" have been carefully evaluated and found to be insignificant and of no practical importance. They were assessed to be <u>much less</u> than one case of minor inconvenience, such as mild diarrhea, per million years per world population (e.g., "Biomedical Scientists and Public Policy", H. H. Fudenberg and V. L. Melnick, (eds.), Plenum Press, New York, 1978, p. 112-113). A very comprehensive volume, which documents the absence of any significant dangers and the lack of the necessity for any regulations, and which calls for dismantling the so-called NIH Guidelines ("Recombinant DNA and Genetic Experimentation", J. Morgan and W. J. Whelan, eds., Pergamon Press, Oxford and New York, 1979) was recently published.

(3) Another important fact, which was not clearly recognized when the Guidelines were proposed and, therefore, makes the present regulations totally unnecessary, is that the recombinant DNA technique has an inherent "early-warning system", and thus cannot result in any unexpected serious epidemics or environmental pollution. Let me explain this principle, which was also outlined in T.I.B.S. (Vol. 4, 1979, p. N190).

(a) To convert an innocuous laboratory strain into a dangerous epidemic pathogen or environmental pest, if that could ever be accomplished, many well-designed genetic steps would be necessary.

(b) During usual cloning, however, only one or a very few such steps could inadvertantly occur.

(c) An event that consists of only one or a few steps is vastly more probable than a multi-step event.

(d) If one imagines that any harmful organisms could be inadvertently produced during cloning, then the very weak pathogens or pests, which by chance acquired only one or a very limited number of genetic changes, would be vastly more probable than any truly dangerous epidemic organisms.

(e) Thus, such very weak pathogens or pests, if ever produced, would provide an ample early warning in the form of some minor afflictions like mild diarrhea, skin rash, or discoloration in a water bath.

(f) One could calculate that many decades, centuries or millenia would be required for further inadvertent conversion of such weak "early-warning" pests into some seriously detrimental organisms. Therefore, there would be ample time to consider the reinstatement of the Guidelines after some early warning should be reported and confirmed.

(4) One could ask whether such an early warning would ever be detected. There is little doubt that there would be more than enough eager individuals who are highly concerned about their health or the environment, and who would report any suspicious afflictions, if ever occurring, to the IBC or ORDA. The verification of such an event and a certainity that it has something to do with recombinant DNA should not be too difficult, since the laboratories working with recombinant DNA have quite detailed data permitting the characterization of cloned DNA and vectors by a variety of molecular diagnostic techniques.

(5) One could prepare a long list of many harmful effects of the present regulations (see, e.g., T.I.B.S. Vol. 3, (1978), pp. N243-N247). Therefore, it is imperative to promptly suspend the present NIH Guidelines and regulations and store them in the archives (or "preserve them under glass" as suggested by the Director of NIH; "Recombinant DNA and Genetic Experimentation", J. Morgan and W. J. Whelan, eds., Pergamon Press, Oxford and New York, 1979, p. 156) until some well substantiated early warning should materialize.

(6) If it is unknown whether a given human activity results in benefits or harm, certainly there is no logical reason to restrict or regulate such activity. Since in the case of recombinant DNA the known benefits are high and no practical risks are known or are insignificant, any restrictions or bureaucratic regulations are clearly harmful and highly unjustified. The present NIH Guidelines, while concentrating on imaginary or insignificant risks, detract from the important environmental and public heatlh concerns; thus, by misdirecting funds and effort, the NIH Guidelines are detrimental to the legitimate regulatory efforts designed to enhance our health and environment.

I believe that even without presenting any further evidence, the above arguments for suspending the regulations, including all attending bureaucracy, is overwhelming and conclusive. I realize, however, that this proposed major action will spawn a certain amount of discussion and maybe opposition from the persons with vested administrative, economical or political interests or from the arch-conservative elements. However, I am encouraged by the previous major actions and with the ultimate acceptance of my previous suggestions, even after I was no longer a member of RAC. As an example, I could cite my previous proposal (see Recombinant DNA Research, Vol. 3, Appendices A161-164) that, when first formulated and formally presented in 1977, it was considered outlandish and hardly worth consideration. However, this early proposal became incorporated into the present Guidelines in 1980 with hardly any differences from my original formulation, namely "that with only a few exceptions, one should exclude from the Guidelines all experiments employing EK1 and EK2 host-vector combinations that carry novel recombinant DNA...[and that] only a very simple registration of these EK1 and EK2 experiments [should perhaps be required]". Encouraged by this laudable responsiveness of RAC, NIH and DHEW, I urge you to announce my present proposal (in the form of this letter) in the next Federal Register, include it in the RAC agenda, consider it in a special subcommittee, and finally approve it. I sincerely hope that the logic of this proposal and the best interests of Society will ultimately prevail.

Sincerely,

Waclaw Szybalski
Professor of Oncology
Former Member of RAC in 1974-1977

WS:kt

Enclosures:

(1) W. Szybalski, 1978. Dangers of regulating the recombinant DNA technique. Trends in Biochem. Sciences 3(1978)N243-N247.

(2) W. Szybalski, 1979-letter. Risks of recombinant DNA regulations. Nature, 278(1979)10.

(3) W. Szybalski, 1979-letter. DNA research as 'high-intensity' science; Diverting the public's attention? TIBS 4(1979)N190.